**REMARKS**

Claims 1-4 currently appear in this application. The Office Action of June 28, 2005, has been carefully studied. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicants respectfully request favorable reconsideration, entry of the present amendment, and formal allowance of the claims.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Reich et al., U.S. Patent No. 5,288,489.

This rejection is respectfully traversed. The claims have now been amended to recite the binding assay so as to more explicitly define how the specific heparin-binding fractions are selected for providing the plasminogen fragments of the present invention.

The fragment of the present invention, Lys-Lysine Binding site I, hereinafter referred to as "Lys-LBS-I", has the following characteristics:

1. It has a molecular weight of 38 kDa.

2. It is not glycosylated.

3. It binds intensely to heparin while it binds less intensely to heparin or heparin-like substances under physiological (isotonic) conditions, *e.g.*, at

around neutral pH, but it binds intensely to heparin under non-physiological conditions, *e.g.*, at a lower environmental pH, such as in the region of a tumor; and

4. It has the ability to inhibit lung tumor metastasis and lung tumor growth, but it has substantially no activity in inhibiting growth of endothelial cells of blood vessels.

The fragment of the present invention is prepared by the following method:

a. preparing Lys-Plasminogen from human plasminogen either by adding plasmin to a solution of human plasminogen or by incubating human plasminogen in the presence of tranexamic acid to autolysis;

b. treating the Lys-plasminogen obtained in step (a) with elastase to produce fractions of the fragment consisting of Kringle 1 to Kringle 3;

c. subjecting the fractions of the fragment consisting of Kringle 1 to Kringle 3 obtained in step (b) to heparin affinity chromatography for selecting heparin-binding fractions to obtain said plasminogen fragment that binds to heparin.

There is nothing in Reich et al. with respect to obtaining only fractions of Kringle 1-Kringle 3 by subjecting the fragment to affinity chromatography for selecting heparin-binding fractions to obtain a fragment that binds to heparin. The present invention thus is limited to a specific fragment with specific properties. There is nothing in Reich et al. regarding the specific properties of the fragment of the present invention nor the method of making the fragment so that it possesses these properties.

Unlike the fragments of Reich et al., the fragments of the present invention have substantially no activity for inhibiting growth of endothelial cells of blood vessels. The biological activity of the fragment claimed herein is based on its special high-order structure that can be established by Lys-LBS-I with N-terminal lysine-78 without glycosylation. This special high-order structure is associated with the ability of the fragment to bind heparin strongly.

The claims now set forth a heparin-binding assay to obtain the fragments that bind heparin.

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

Respectfully submitted,

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